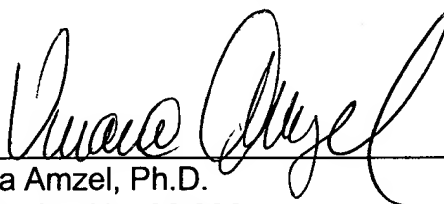


In view of the foregoing, it is believed that this application is in condition for examination on the merits, and for allowance. Early notice of that effect is hereby solicited.

Respectfully submitted.

EPIGENESIS PHARMACEUTICALS, INC.



Viviana Amzel, Ph.D.  
Registration No. 30,930  
Attorney for the Applicant

September 28, 2001  
Date

7 Clarke Drive  
Cranbury, NJ 08512  
609-409-3035 Legal Dept Phone  
413-254-9245 Legal Dept Fax  
vamzel@epigene.com E-mail

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SIGNATURE

GGATATAGGT TTCCAATTAA GTACATGGTC AAGTATTAAC AGCACAAGTG GTAGGTAAAC ATTAGAATAG  
 GAATTGGTGT TGGGGGGGGG GTTGCAAGA ATATTTTATT TTAATTTTTT GGATGAAATT TTTATCTATT  
 ATATATTAAA CATTCTTGCT GCTGCGCTGC AAAGCCATAG CAGATTGAG GCGCTGTTGA GGACTGAATT  
 ACTCTCCAAG TTGAGAGATG TCTTTGGGTT AAATTAAGAG CCCTACCTAA AACTGAGGTG GGGATGGGGA  
 5 GAGCCTTTGC CTCCACCATT CCCACCCACC CTCCCCTTAA ACCCTCTGCC TTTGAAAGTA GATCATGTTC  
 ACTGCAATGC TGGACACTAC AGGTATCTGT CCCTGGGCCA GCAGGGACCT CTGAAGCCTT CTTTGTGGCC  
 TTTTTTTTTT TTCATCCTGT GGTTTTTCTA ATGGACTTTC AGGAATTTTG TAATCTCATA ACTTTCCAAG  
 CTCCACCACT TCCTAAATCT TAAGAACTT AATTGACAGT TTCAATTGAA GGTGCTGTTT GTAGACTTAA  
 10 CACCCAGTGA AAGCCCAGCC ATCATGACAA ATCCTTGAAT GTTCTCTTAA GAAAATGATG CTGGTCATCG  
 CAGCTTCAGC ATCTCCTGTT TTTTGATGCT TGGCTCCCTC TGCTGATCTC AGTTTCCTGG CTTTTCTCC  
 CTCAGCCCCT TCTACCCCT TTGCTGTCCT GTGTAGTGAT TTGGTGAGAA ATCGTTGCTG CACCCCTCCC  
 CCAGCACCAT TTATGAGTCT CAAGTTTTAT TATTGCAATA AAAGTGCTTT ATGCCCGAAT TC-3' (FRAG.NO:.)  
 (SEQ. ID NO:2497)  
 5' GCCGCCGCCA TGGGAGTGCA GGTGGAAACC ATCTCCCCAG GAGACGGGCG CACCTTCCCC AAGCGCGGCC  
 15 AGACCTGCGT GGTGCACTAC ACCGGGATGC TTGAAGATGG AAAGAAATTT GATTCTCCC GGGACAGAAA  
 CAAGCCCTTT AAGTTTATGC TAGGCAAGCA GGAGGTGATC CGAGGCTGGG AAGAAGGGGT TGCCAGATG  
 AGTGTGGGTC AGAGAGCCAA ACTGACTATA TCTCCAGATT ATGCCTATGG TGCCACTGGG CACCCAGGCA  
 TCATCCACC ACATGCCACT CTCGTCTTCG ATGTGGAGCT TCTAAACTG GAATGACAGG AATGGCCTCC  
 20 TCCCTTAGCT CCCTGTTCTT GGATCTGCCR TGGAGGGATC TGGTGCTCC AGACATGTGC ACATGARTCC  
 ATATGGAGCT TTTCCTGATG TTCCACTCCA CTTTGTATAG ACATCTGCCC TGAATGATG TGTCTGTCA  
 CTCAGCTTTG CTTCCGACAC CTCTGTTTCC TCTTCCCTT TCTCCTCGTA TGTGTGTTA CCTAACTAT  
 ATGCCATAAA CCTCAAGTTA TTCA-3' (FRAG. NO:.) (SEQ. ID NO:2498)

wherein B is adenosine, or, more preferably, replaces adenosine and is an “equivame\\lent” or a “universal”  
 base, and adenosine A<sub>2a</sub> receptor agonist or only minimally antagonist, an adenosine A<sub>2b</sub> receptor antagonist,  
 25 an adenosine A<sub>3</sub> receptor antagonist, or an adenosine A<sub>1</sub> receptor antagonist. Similarly, adenosine (A) may  
 always be replaced by an “alternative”, “equivalent” and/or “universal” base having a small fraction,  
 preferably less than 0.3 of the activity of adenosine at the adenosine receptor(s), as described above.

In one preferred embodiment, the links between neighboring mononucleotides are phosphodiester  
 links. In another preferred, at least one mononucleotide phosphodiester residue of the anti-sense  
 30 oligonucleotide(s) is substituted by a methylphosphonate, phosphotriester, phosphorothioate,  
 phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate,  
 sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, 2'-O-methyl,  
 methylene(methylimino), methyleneoxy (methylimino), phosphoramidate residues, and combinations thereof.  
 The oligos having one or more phosphodiester residues substituted by one or more of the other residues are  
 35 generally longer lasting, given that these residues are more resistant to hydrolysis than the phosphodiester  
 residue. In some cases up to about 10%, about 30%, about 50%, about 75%, and even all phosphodiester  
 residues may be substituted (100%). Typically, the multiple target anti-sense oligonucleotide (oligo) of the  
 invention comprises at least about 7 mononucleotides, in some instances up to 60 and more mononucleotides,  
 preferably about 10 to about 36, and more preferably about 12 to about 21 mononucleotides. However, other  
 40 lengths are also suitable depending on the length of the target macromolecule. Examples of the MTA oligos of  
 the invention are provided in Table 3 below, which includes ninety-four sequences (SEQ ID NOS.: 2316  
 through 2410).

Table 3: MTA Oligos, Location Targeted & Target

| MTA Oligo                             | SEQ. ID<br>No. | Location    | Compound<br>Targeted | Target |
|---------------------------------------|----------------|-------------|----------------------|--------|
| <b>HUMNFKBP65A AS</b>                 |                |             |                      |        |
| CCC GGC CCC GCC TCG TGC C             | 3019           | 5'=1        | EPI 2192             |        |
| CGT CCB TGC CGC GGG CCC               | 3020           | 5'=28 (AUG) | EPI 2193             |        |
| GCC CCG CTG CTT GGG CTG CTC TGC CGG G | 3021           | 5'=65       | EPI 2194             |        |
| 50 TCT GTG CTC CTC TCG CCT GGG        | 3022           | 5'=137      | EPI 2195             |        |
| TGG TGG GGT GGG TCT TGG TGG           | 3023           | 5'=159      | EPI 2196             |        |
| CTG TCC CTG GTC CTG TG                | 3024           | 5'=196      | EPI 2197             |        |
| GGT CCC GCT TCT TC                    | 3025           | 5'=362      | EPI 2198             |        |
| GGG GTT GTT GTT GGT CTG G             | 3026           | 5'=401      | EPI 2199             |        |
| 55 TGT CCT CTT TCT GC                 | 3027 [3026]    | 5'=656      | EPI 2200             |        |
| GCC TCG GGC CTC CC                    | 3028 [3027]    | 5'=697      | EPI 2201             |        |
| GGC TGG GGT CTG CGT                   | 3029 [3028]    | 5'=769      | EPI 2202             |        |

|    |                                     |            |          |  |
|----|-------------------------------------|------------|----------|--|
| 5  | GGC CGG GGG TCG GTG GGT CCG CTG     | 3030[3029] | 5'=953   | EPI 2203                                   |
|    | GGG CTG GGG TGC TGG CTT GGG G       | 3031[3030] | 5'=1022  | EPI 2204                                   |
|    | GGG GCT GGG GCC TGG GCC             | 3032[3031] | 5'=1208  | EPI 2205                                   |
|    | GCC TGG GTG GGC TTG GGG GC          | 3033[3032] | 5'=1272  | EPI 2206                                   |
|    | GCT GGG TCT GTG CTG TTG CC          | 3034[3033] | 5'=1362  | EPI 2207                                   |
| 10 | GTT GTG TGG GGG GCC                 | 3035[3034] | 5'=1451  | EPI 2208                                   |
|    | GCT GGG TCG GGG GGC CTC TGG GCT GTC | 3036[3035] | 5'=1511  | EPI 2209                                   |
|    | GCC CCG GGG CCC CC                  | 3037[3036] | 5'=1550  | EPI 2210                                   |
|    | TGG CTC CCC CCT CC                  | 3038[3037] | 5'=1772  | EPI 2211                                   |
|    | GCT CCC CCC TTT CC                  | 3039[3038] | 5'=1863  | EPI 2212                                   |
| 15 | CGG ACG AAG ACA GAG A               | 3040[3039] | 5'=1979  | EPI 2213                                   |
|    | GGC TTT GTG GGC TC                  | 3041[3040] | 5'=2011  | EPI 2214                                   |
|    | GCC TGC TCT CCC CC                  | 3042[3041] | 5'=2312  | EPI 2215                                   |
|    | CCC GGC CCC GCC BCG BBC C           | 3043[3042] | intron   | EPI 2192-01A HSU50136C4Synth               |
|    | CCC GGC CCC GCC BCG                 | 3044[3043] | intron   | EPI 2192-01B                               |
| 20 | CCC GGC CCC GCC BCG BBC C           | 3045[3044] | 5'untr   | EPI 2192-02A HUMLIPOX5LO                   |
|    | CCC GGC CCC GCC BCG                 | 3046[3045] | 5'untr   | EPI 2192-02B                               |
|    | CCC GBC CCC GCC TCB BG              | 3047[3046] | trans    | EPI 2192-03A HSNFKBS Subunit               |
|    | CCC GBC CCC GCC TC                  | 3048[3047] | trans    | EPI 2192-03B                               |
|    | CCG GCC CCG CCT C                   | 3049[3048] | 5'untr   | EPI 2192-04 TGF $\alpha$ R1                |
| 25 | CCC GBB CCC GCB TBG TGC C           | 3050[3049] | 5'trans  | EPI 2192-05A HSUS8198I1 enhan              |
|    | CCC GCB TBG TGC C                   | 3051[3050] | 5'untr   | EPI 2192-05B                               |
|    | CCC GGB CCC BCC BBG TGC C           | 3052[3051] | 3'trans  | EPI 2192-06 HSVECAD                        |
|    | CBG BBC CCG CCT CGT GCC             | 3053[3052] | intron   | EPI 2192-07A NFKB2                         |
|    | C CCG CCT CGT GCC                   | 3054[3053] | intron   | EPI 2192-07B NFKB2                         |
| 30 | CCG GCB CCG CCT CBT GCC             | 3055[3054] | 5'trans  | EPI 2192-08 Carboxypep                     |
|    | CCG GCC CCG CCB CBT GCC             | 3056[3055] | 3'trans  | EPI 2192-09 HumADRA2C $\beta$ 2AdrKid      |
|    | CCC GBC CCC GBC TCG                 | 3057[3056] | 5'untrs  | EPI 2192-10 HUMFK506B                      |
|    | CCC GGC CBC GBC TCG                 | 3058[3057] | 5'untrs  | EPI 2192-11 HSNBARKS1 $\alpha$ AdrKin      |
|    | CCC GGC CCB GCC TBG                 | 3059[3058] | 5'UTR    | EPI 2192-12 HSNFXN1 (NFKB1)                |
| 35 | CCC GGC BCB GBC TCG TBC C           | 3060[3059] | 3'UTR    | EPI 2192-13 HSILF(transcrp. Factor ILF)    |
|    | CCC GGC CCC GCC BCG                 | 3061[3060] |          | EPI-2192-14 NFKB/C4Syn/5-LO/TGFBrecl MTA   |
|    | CCC GGC CCC GCC BCG                 | 3062[3061] |          | EPI-2192-15NFKB/C4Syn/5-LOMTA              |
|    | TCC BTG CCG CGG GC                  | 3063[3062] | 3' trans | EPI-2193-01 METOncogene                    |
|    | TCC BTG CCB CGG GCC                 | 3064[3063] | 3' trans | EPI-2193-02 HSFGR2 (IG)                    |
| 40 | TCC BTG CCB CGG GCC                 | 3065[3064] | mid cod  | EPI-2193-03 5-LO                           |
|    | TCC BTG CCB CBG GCC                 | 3066[3065] | mid cod  | EPI-2193-04 HUMTK14                        |
|    | GTC CBT GBC GCG G                   | 3067[3066] | 3'trans  | EPI-2193-05 HUMTNFR                        |
|    | TC CBT GBC GCG GG                   | 3068[3067] | AUG      | Probl.HUMPTCH cardiacK+channel             |
|    | TCT GBG CTC CTC TBB CCT GGG         | 3069[3068] | intr     | EPI-2195-01 humCSPAcytotox. Ser. Protease  |
| 45 | CTG TGC BCC TBB CBC CTG GG          | 3070[3069] | intr     | EPI-2195-02 HSINOSX08induc.NOS             |
|    | TGT GBT CCB CTB GBC TGG G           | 3071[3070] |          | EPI-2195-03 HUMACHRM2musc.m2 acetylch.rec. |
|    | TCT GTB CTC BBC TCB CCT G           | 3072[3071] |          | EPI-2195-04 s86371s1 Neurokinin3Recept     |
|    | TGC TCC TCB CBB CTG GG              | 3073[3072] |          | EPI-2195-05 HUMMIP1 Amacro                 |
|    | inflam.factor                       |            |          |  |

Table 3: MTA Oligos, Location Targeted &amp; Target (Cont'd)

| MTA Oligo                  | SEQ. ID No. | Location      | Compound Targeted | Target   |
|----------------------------|-------------|---------------|-------------------|--|
| 5 CTC CTC TBG CCT GG       | 3074 [3073] |               | EPI-2195-06       | HSNBARKS4  |
| GTG CTC CBB TCB BCT GGG    | 3075 [3074] |               | EPI-2195-07       | $\beta$ -Adr Rec Kinase                          |
| GTG CBC CBB TCB CCT GGG    | 3076 [3075] |               | EPI-2195-08       | HSTNFR2SO6TNF R2                                 |
|                            |             |               |                   | humfkbp fk506 binding prot.                      |
| 10 TCT GTG CBC CTC TBG BCT | 3077 [3076] | exon          | EPI-2195-09       | HSNBARKS16-Adr. Recept. Kinase                   |
| CTG TBB TCC TBB CBC CTG G  | 3078 [3077] | intron        | EPI-2195-10       | HUMIL8   |
| TGT GCT BBT CBC BCB TGG G  | 3079 [3078] |               | EPI-2195-11       | HSU50157 PDE4                                    |
| GTG CBC CBC TCB CCT G      | 3080 [3079] | intron/exon   | EPI-2195-12       | IL-2 R   |
| CTG TGC BCC TCT C          | 3081 [3080] | 3'UTR         | EPI-2203-05       | IL-6 R HSIL6R                                    |
| 15 CBG TGC BCC BCT CBC CTG | 3082 [3081] | intr/ex       | EPI-2203-06A      | HSIL2rG6   |
| G TGC BCC BCT CBC CTG      | 3083 [3082] | intr/ex       | EPI-2203-06B      | HSIL2rG6   |
| CBC CTC TCB CCT GGG        | 3084 [3083] | coding        | EPI-2203-07A      | HUMIL71  |
| C CTC TCB CCT GGG          | 3085 [3084] | coding        | EPI-2203-07B      | IL-7 HUMIL71                                     |
| GCT CCB CTC GCC T          | 3086 [3085] | coding        | EPI-2203-08       | IL-6 R HSI6REC                                   |
| 20 TGC TCC TCB CGC C       | 3087 [3086] | intron PDGF A | EPI-2303-09       | Chain HUMPDGFAB                                  |
| GTT GTT GBT CTG G          | 3088 [3087] | 3'utr         | EPI-2199-01       | GATA-4Transcrip. Factor for IL-5                 |
| GGT TGB BBT TGG TCT TGG    | 3089 [3088] | Coding        | EPI-2199-02       | TNF $\alpha$ HUMTNFA                             |
| GGT TGT TGB TGB TCT G      | 3090 [3089] | Far 5'UTR     | EPI-2199-03       | HSSUBP1G(Sub Pr)                                 |
| 25 GGG TTB BBG TTG BTC TGG | 3091 [3090] | Coding        | EPI-2199-04       | NeutrophilAdh. R HUMNARIA                        |
| GGG TTB BBG TTG BTC TGG    | 3092 [3091] | HSHM2         | EPI-2199-05       | m2 Muscarinic R                                  |
| TTG TTG TBG BTC TGG        | 3093 [3092] | HUML1CAM      | EPI-2199-06       | L1 LeukAadhProt                                  |
| GGG TBG BBG BGT CCG CTG    | 3094 [3093] | coding        | EPI-2203-01       | HUMGATA2A  |
| 30 GGG TCB GBG GBT CBG CTG | 3095 [3094] | S71424S2      | EPI-2203-02       | IGE eps  |
| GGG TBG GTG GGT C          | 3096 [3095] | coding        | EPI-2203-03       | HSGCSFR2   |
| GGG TCG GBG GGT CBG C      | 3097 [3096] | HUMITGF       | EPI-2203-04       | TGF $\alpha$ 3                                   |
| GGG TGG GCT T              | 3098 [3097] | HUMNK65PRO    | EPI-2206-01       | NFKB/NK & TCell                                  |
| 35 GGG TGG GCT TGG G       | 3099 [3098] | HUMPEREEB     | EPI 2206-02       | Activating Prot NFKB/Prostagl. EP3 Rec           |
| CCTGGGTGGGBBTGGG           | 3100 [3099] |               | EPI 2206-03       | HSNF2B/GCSF NFKB/GranuLocCSF/Transcr. FactorNF2B |
| 40 CCTGGBTGGGCBTGGG        | 3101 [3100] |               | EPI-2206-04       | HUMLAP/NFKB Leuk. Adhes. Prot                    |
| GCCTGBGTGBBCTTGGG          | 3102 [3101] |               | EPI2206-05        | NFKB/Endothel N2 S63833                          |
| 45 CCCAVGVCCVCCAGGC        | 3103 [3102] |               | EPI 2206-06       | NFKBAS13/B Lymph SerThrProt. Kinase              |
| AGCCACCCAGGC               | 3104 [3103] |               | EPI2206-07        | NFKBAS13/GCSF1 HSGCSFR1Rec                       |
| 50 BCCTGGGTGGGCTB          | 3105 [3104] |               | EPI2206-08        | NFKBAS13/GCSF1/NK7TCELLACT. Prot                 |
| GGTGGGCTTGGG               | 3106 [3105] |               | EPI 2206-09       | NFKBAS13/HSTGFB1 TGFB                            |
| CCBBGGTGGGCTTGGG           | 3107 [3106] |               | EPI 2206-10       | NFKBAS13/HSTGFB1 TGFB1                           |
| 55 CTGGGTGGGBBTGGG         | 3108 [3107] |               | EPI 2206-11       | NFKBAS13/HSGCSFR1 GCSFR1                         |
| CCBGGGTGGGCTTGG            | 3109 [3108] |               | EPI 2206-12       | NFKBAS13/HUMCD30A LymphActAntigCoding            |
| GGGTGGGCTTGG               | 3110 [3109] |               | EPI-2206-12B      | NFKBAS13/HUMCD30A                                |
| 60 CCTGBGTGBGCBTGGG        | 3111 [3110] |               | EPI 2206-13       | NFKBAS13/HUMCAM1V Vasc. Endoth. Cell Adh. Molec  |

B: Universal Base

The MTA oligos of Table 3 are suitable for use with two or more of the targets listed in Table 4 below.